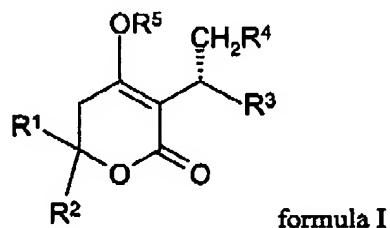


REMARKS

Claims 1-22 are pending.

Claim 1, which is representative of the subject matter claimed, reads as follows:

1. A process for preparing a compound of the formula I:



wherein

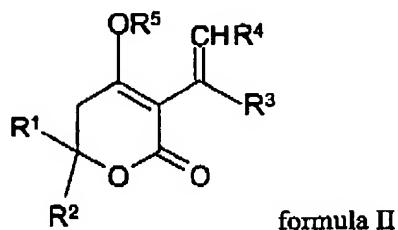
$R^1$  and  $R^2$  independently of one another denote hydrogen or a group which is selected from among the group consisting of  $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_8$ -cycloalkyl,  $C_6$ - $C_{10}$ -aryl and  $C_1$ - $C_4$ -alkylene- $C_6$ - $C_{10}$ -aryl, optionally with one, two or three substituents, selected from the group consisting of OH, NH<sub>2</sub>, NH-CO-CH<sub>3</sub> or N(-CO-CH<sub>3</sub>)<sub>2</sub>, halogen,  $C_1$ - $C_4$ -alkoxy and CF<sub>3</sub>, while  $R^1$  and  $R^2$  do not simultaneously have the same meaning;

$R^3$  denotes an aryl substituted in the meta position, which optionally comprises at least one other substituent, the substituents being selected from the group consisting of F, Cl, Br, I, OH, O-SO<sub>2</sub>-CF<sub>3</sub>, NO<sub>2</sub>, NH<sub>2</sub>, NH-SO<sub>2</sub>-(4-trifluoromethylpyridin-2-yl), N(-CH<sub>2</sub>-aryl)<sub>2</sub>, NY<sub>1</sub>Y<sub>2</sub> with Y<sub>1</sub> and Y<sub>2</sub> selected from H, COO-alkyl, COO-CH<sub>2</sub>-aryl, CO-alkyl and CO-aryl;

$R^4$  is selected from the group consisting of H and  $C_1$ - $C_8$ -alkyl; and

$R^5$  is selected from the group consisting of H, Si(CH<sub>3</sub>)<sub>3</sub>, Li, Na, K, Cs, N(R')<sub>4</sub>, while all the R' groups may be identical or different and are selected from  $C_1$ - $C_8$ -alkyl and CH<sub>2</sub>-aryl;

which process comprises hydrogenating a compound of the formula II



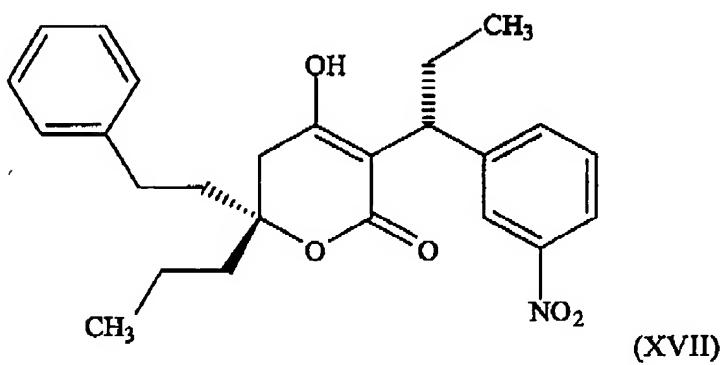
wherein the groups R<sup>1</sup> to R<sup>5</sup> are as previously defined in this claim, in the presence of a catalyst which contains at least one ligand in the form of a chiral 1,2-bis(phospholano)maleic anhydride.

Claims 1-22 stand rejected under 35 USC 103(a) as being unpatentable over Gage et al. (WO 0055150) in view of Holz et al. (J. Org. Chem. 2003, 68, 1701-1707).

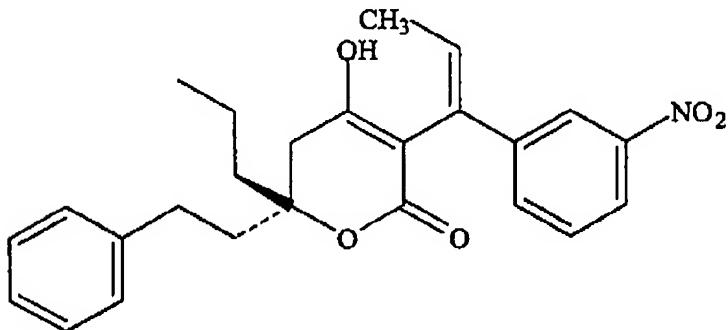
The action states, "the former [WO 0055150] discloses the same asymmetric hydrogenation using the corresponding bis-(dimethyl-phospholane) benzene catalyst, commonly termed Me-DuPHOS. See Ex. 17 wherein [(1,5-cyclooctadiene)rhodium(I)-1,2-bis-(2R,5R)dimethyl-phospholano]benzene]tetrafluoroborate the chemical name of Me-DuPHOS is given. Note that the 3alpha(R) enantiomer is stereoselectively produced."

It should be noted that the reference to WO 0055150 would appear to be an error because this document does not contain an "Example 17". It is believed that the intended reference is WO 9912919 (hereinafter called "Gage II"). The latter contains an Example 17 which describes relevant subject matter. Thus, the rejection will be treated as being based upon Gage II (WO 9912919) in view of Holz et al.

Example 17 of Gage II describes the synthesis of [3α(R),6(R)]5,6-dihydro-4-hydroxy-3-[1-(3-nitrophenyl)propyl]-6-[1-(2-phenyl)ethyl]-6-propyl-2H-pyran-2-one



by the hydrogenation of [3  $\alpha$  (R),6(R)]5,6-Dihydro-4-hydroxy-3-[(Z)-1-(3-nitrophenyl)propenyl]-6-[1-(2-phenyl)ethyl]-6-propyl-2H-pyran-2-one



using [(1,5-cyclooctadiene)rhodium(I)-1,2-bis-(2R,5R)-dimethylphospholano]benzene]tetrafluoroborate (Me-DuPHOS-Rh) as catalyst.

It is conceded that the sole difference between the claimed invention and the prior art synthesis of Example 17 of Gage II is that the invention employs a catalyst which includes a chiral 1,2-bis(phospholano)maleic anhydride as its ancillary ligand, with MalPHOS being specified as ligand in claim 15, whereas Gage II employs a catalyst which includes 1,2-bis-(2R,5R)-dimethylphospholano]benzene (Me-DuPHOS) as the ligand.

It appears to be the Examiner's position that the Holz et al. reference supplies the motivation to replace the Me-DuPHOS ligand used in the synthesis of Gage II with MalPHOS, thus bridging the gap between the prior art and the invention. The applicants do not agree that this is a correct position.

If Holz et al. did, in fact, show that MalPHOS is always a better ligand than Me-DuPHOS, regardless of the substrate to be acted upon by the catalyst it might be necessary to concede the Examiner's point. However, this is not what Holz et al. teach.

Holz et al. hydrogenated a variety of substrates using Rhodium as catalyst and both MalPHOS and Me-DuPHOS as ligands. For some substrates better enantioselectivity was achieved using MalPHOS, while for other substrates better enantioselectivity was achieved using Me-DuPHOS. In the Conclusion of their paper they state, "Our results clearly demonstrate that for each substrate, an individual catalyst has to be identified in order to induce the maximum enantioselectivity."

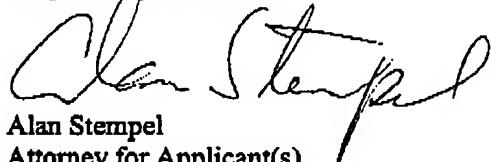
Had Holz et al. employed substrates bearing structural similarity to the compounds of formula II of the present invention, and shown that for such compounds MalPHOS is the preferable ligand, the reference might supply the motivation to replace Me-DuPHOS with MalPHOS, as the Examiner suggests. But the substrates hydrogenated

by Holz et al. are structurally quite unlike the compounds of formula II of the present invention.

| At best, Holz et al. merely inform those of skill in the art of the availability of MalPHOS, as a new catalytic ligand. However, since Holz et al. clearly show that MalPHOS is sometimes superior to Me-DuPHOS as a ligand, and sometimes inferior – it depends upon the substrate – and since the substrates of Holz et al. are quite unlike those employed in the hydrogenation of the claimed invention, the Holz reference would not provide the motivation to replace the Me-DuPHOS ligand used by Gage II with MalPHOS.

It is thus urged that the rejection of the claims lacks a sound basis and should be withdrawn.

Respectfully submitted,



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